A Study to Evaluate Efficacy, Safety, and Immunogenicity of mRNA-1273 Vaccine in Adults Aged 18 Years and Older to Prevent COVID-19

ClinicalTrials.gov Identifier: NCT04470427

Recruitment Status : Active, not recruiting
First Posted : July 14, 2020
Last Update Posted : June 10, 2021

Sponsor:
ModernaTX, Inc.

Collaborators:
Biomedical Advanced Research and Development Authority
National Institute of Allergy and Infectious Diseases (NIAID)

Information provided by (Responsible Party):

ModernaTX, Inc.

Study Description

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Brief Summary:

The mRNA-1273 vaccine is being developed to prevent COVID-19, the disease resulting from Severe Acute Respiratory Syndrome coronavirus (SARS-CoV-2) infection. The study is designed to primarily evaluate the efficacy, safety, and immunogenicity of mRNA-1273 to prevent COVID-19 for up to 2 years after the second dose of mRNA-1273.

Condition or disease	Intervention/treatment	Phase
SARS-CoV-2	Biological: mRNA-1273 Biological: Placebo	Phase 3

Detailed Description:

This is a 2-part Phase 3 study, with Part A (Blinded Phase) and Part B (Open-label Observational Phase). Participants in Part A are blinded to their treatment assignment, with participants receiving either 2 active mRNA-1273 vaccine doses or placebo. Part B of the study is designed to offer participants to be unblinded so that participants who received placebo in Part A can request 2 doses of open-label mRNA-1273 vaccine. Additionally, participants who choose to be unblinded and was only able to receive 1 dose of mRNA-1273 due to administrative reasons, can choose to receive the second dose of mRNA-1273 during Part B.

Please access www.modernatx.com/cove-study for additional information, such as Study Overview, Participation, and Site Locations along with contact numbers for each location for the study.

Study Design

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Study Type : Interventional (Clinical Trial)

Actual Enrollment :	30420 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Masking Description:	Part A is observer-blind. During Part B participants may request to be unblinded by scheduling a Participant Decision clinic visit.
Primary Purpose:	Prevention
Official Title:	A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older
Actual Study Start Date :	July 27, 2020
Estimated Primary Completion Date :	October 27, 2022
Estimated Study Completion Date :	October 27, 2022

Arms and Interventions

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Arm	Intervention/treatment
Experimental: mRNA-1273 Part A: Participants will receive 1 intramuscular (IM) injection of 100 microgram (ug) mRNA-1273 on Day 1 and on Day 29. Part B: Participants who choose to be unblinded and received mRNA-1273-matching placebo during Part A, will receive 1 IM injection of 100 ug mRNA-1273 on Day 1 and Day 29, if the participant chooses. Participants who choose to be unblinded and was only able to receive 1 dose of mRNA-1273 due to administrative reasons, will receive 1 IM injection of 100 ug mRNA-1273 on Day 1,	Biological: mRNA-1273 Sterile liquid for injection Biological: Placebo 0.9% sodium chloride (normal saline) injection

Arm	Intervention/treatment
if the participant chooses.	
Placebo Comparator: Placebo Part A only: Participants will receive 1 IM injection of mRNA-1273-matching placebo on Day 1 and on Day 29, if the participant chooses.	Biological: Placebo 0.9% sodium chloride (normal saline) injection

Outcome Measures

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Primary Outcome Measures :

1. Efficacy: Number of Participants with a First Occurrence of COVID-19 Starting 14 Days after Second Dose of mRNA-1273 [Time Frame: Part A only: Day 43 (14 days after second dose) up to Day 759 (2 years after second dose)]
2. Safety: Number of Participants with Adverse Events (AEs) or Medically Attended AEs (MAAEs) Leading to Withdrawal [Time Frame: Up to Day 759 (2 years after second dose)]
3. Safety: Number of Participants with Solicited Local and Systemic Adverse Reactions (ARs) [Time Frame: Part A only: Up to Day 8 (7 days after first dose) and up to Day 36 (7 days after second dose)]
4. Safety: Number of Participants with Unsolicited AEs [Time Frame: Up to Day 57 (28 days after each dose)]
5. Safety: Number of Participants with Serious AEs (SAEs) [Time Frame: Up to Day 759 (2 years after second dose)]

Secondary Outcome Measures :

1. Number of Participants with a First Occurrence of Severe COVID-19 Starting 14 Days after Second Dose of mRNA-1273 or Placebo [Time Frame: Day 43 (14 days after second dose) up to Day 759 (2 years after second dose)]

   Clinical signs indicative of severe COVID-19 as predefined for the study.

2. Number of Participants with a First Occurrence of Either COVID-19 or SARS-CoV-2

Infection regardless of symptomatology or Severity Starting 14 Days after Second Dose of mRNA-1273 or Placebo [Time Frame: Day 43 (14 days after second dose) up to Day 759 (2 years after second dose)]

Clinical signs indicative of COVID-19 and SARS-CoV-2 Infection as predefined for the study.

3. Number of Participants with a Secondary Case Definition of COVID-19 Starting 14 days after Second Dose of mRNA-1273 or Placebo [Time Frame: Day 43 (14 days after second dose) up to Day 759 (2 years after second dose)]

   Clinical signs indicative of secondary case definition of COVID-19 as predefined for the study.

4. Number of Participants with a First Occurrence of COVID-19 Starting 14 days after First Dose of mRNA-1273 or Placebo [Time Frame: Day 43 (14 days after first dose of the Blinded Phase) up to Day 759 (2 years after second dose)]

   Clinical signs indicative of COVID-19 as predefined for the study.

5. Number of Participants with a First Occurrence of COVID-19 Starting 14 days after Second Dose of mRNA-1273 or Placebo Regardless of Evidence of Prior SARS-CoV-2 Infection [Time Frame: Day 43 (14 days after second dose) up to Day 759 (2 years after second dose)]

   Clinical signs indicative of COVID-19 and SARS-CoV-2 infection as predefined for the study.

6. Number of Participants with a First Occurrence of SARS-CoV-2 Infection in the Absence of Symptoms Defining COVID-19 Starting 14 days after Second Dose of mRNA-1273 or Placebo [Time Frame: Day 43 (14 days after second dose) up to Day 759 (2 years after second dose)]

   Clinical signs indicative of COVID-19 and SARS-CoV-2 infection as predefined for the study.

7. Geometric Mean Titer (GMT) of SARS-CoV-2 Specific Neutralizing Antibody (nAb) [Time Frame: Day 1, Day 29, Day 57, Day 209, Day 394, and Day 759]

8. Geometric Mean Fold Rise (GMFR) of SARS-CoV-2 Specific nAb [Time Frame: Day 1, Day 29, Day 57, Day 209, Day 394, and Day 759]
9. Quantified Levels or GMT of S Protein-Specific Binding Antibody (bAb) [Time Frame: Day 1, Day 29, Day 57, Day 209, Day 394, and Day 759]
10. GMFR of S Protein Specific bAb [Time Frame: Day 1, Day 29, Day 57, Day 209, Day 394, and Day 759]

Eligibility Criteria

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Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	18 Years and older (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	Yes

Criteria

Inclusion Criteria:

- Participants who are at high risk of SARS-CoV-2 infection, defined as adults whose locations or circumstances put them at appreciable risk of exposure to SARS-CoV-2 and COVID-19.
- Understands and agrees to comply with the study procedures and provides written informed consent.
- Able to comply with study procedures based on the assessment of the Investigator.
- Female participants of non-childbearing potential may be enrolled in the study. Non-childbearing potential is defined as surgically sterile (history of bilateral tubal ligation, bilateral oophorectomy, hysterectomy) or postmenopausal (defined as amenorrhea for ≥12

consecutive months prior to Screening without an alternative medical cause). A follicle-stimulating hormone (FSH) level may be measured at the discretion of the Investigator to confirm postmenopausal status.

- Female participants of childbearing potential may be enrolled in the study if the participant fulfills all the following criteria:
  - Has a negative pregnancy test at Screening and on the day of the first dose (Day 1).
  - Has practiced adequate contraception or has abstained from all activities that could result in pregnancy for at least 28 days prior to the first dose (Day 1).
  - Has agreed to continue adequate contraception through 3 months following the second dose on Day 29.
  - Is not currently breastfeeding.
- Healthy adults or adults with pre-existing medical conditions who are in stable condition. A stable medical condition is defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 3 months before enrollment.

Additional Inclusion Criteria for Part B:

Participants who were previously enrolled in the mRNA-1273-P301 study and chose to be unblinded.

Exclusion Criteria:

- Is acutely ill or febrile 72 hours prior to or at Screening. Fever is defined as a body temperature ≥38.0°Celsius/100.4°Fahrenheit. Participants meeting this criterion may be rescheduled within the relevant window periods. Afebrile participants with minor illnesses can be enrolled at the discretion of the Investigator.
- Is pregnant or breastfeeding.
- (Part A Only) Known history of SARS-CoV-2 infection.
- Prior administration of an investigational coronavirus (SARS-CoV, Middle East Respiratory Syndrome [MERS]-CoV) vaccine or current/planned simultaneous participation in another interventional study to prevent or treat COVID-19.
- (Part A Only) Demonstrated inability to comply with the study procedures.
- (Part A Only) An immediate family member or household member of this study's personnel.
- Known or suspected allergy or history of anaphylaxis, urticaria, or other significant adverse reaction to the vaccine or its excipients.
- Bleeding disorder considered a contraindication to intramuscular injection or phlebotomy.

- Has received or plans to receive a vaccine within 28 days prior to the first dose (Day 1) or plans to receive a non-study vaccine within 28 days prior to or after any dose of investigational product (except for seasonal influenza vaccine).
- Has participated in an interventional clinical study within 28 days prior to the day of enrollment.
- Immunosuppressive or immunodeficient state, including human immunodeficiency virus (HIV) infection, asplenia, and recurrent severe infections.
- Has received systemic immunosuppressants or immune-modifying drugs for >14 days in total within 6 months prior to Screening (for corticosteroids ≥20 milligram (mg)/day of prednisone equivalent).
- Has received systemic immunoglobulins or blood products within 3 months prior to the day of Screening.
- Has donated ≥450 milliliters (mL) of blood products within 28 days prior to Screening.

Contacts and Locations

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Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT04470427***

Locations

Show 100 study locations

Sponsors and Collaborators

ModernaTX, Inc.

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More Information

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Additional Information:

Click here to access the website, www.modernatx.com/cove-study, for additional information for the study, such as Study Overview, Participation, and Site Locations, along with contact numbers for each location for the study. EXIT

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, Diemert D, Spector SA, Rouphael N, Creech CB, McGettigan J, Khetan S, Segall N, Solis J, Brosz A, Fierro C, Schwartz H, Neuzil K, Corey L, Gilbert P, Janes H, Follmann D, Marovich M, Mascola J, Polakowski L, Ledgerwood J, Graham BS, Bennett H, Pajon R, Knightly C, Leav B, Deng W, Zhou H, Han S, Ivarsson M, Miller J, Zaks T; COVE Study Group. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021 Feb 4;384(5):403-416. doi: 10.1056/NEJMoa2035389. Epub 2020 Dec 30.

Responsible Party:	ModernaTX, Inc.
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Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:	No

Studies a U.S. FDA-regulated Drug Product:	Yes
Studies a U.S. FDA-regulated Device Product:	No

Keywords provided by ModernaTX, Inc.:

mRNA-1273	Virus Diseases
mRNA-1273 vaccine	Messenger RNA
SARS-CoV-2	COVID-19

SARS-CoV-2 Vaccine
Coronavirus
COVID-19 Vaccine
Moderna